Met Glu Asp Thr Lys Glu Ser Asn Val Lys Thr Phe **Cys** Ser Lys Asn Ile Leu Ala 19

Ile Leu Gly Phe Ser Ser Ile Ile Ala Val Ile Ala Leu Leu Ala Val Gly Leu Thr 38

Gln Asn Lys Ala Leu Pro Glu Asn Val Lys Tyr Gly Ile Val Leu Asp Ala Gly Ser 57

Ser His Thr Ser Leu Tyr Ile Tyr Lys Trp Pro Ala Glu Lys Glu Asn Asp Thr Gly 76

Val Val His Gln Val Glu Glu **Cys** Arg Val Lys Gly Pro Gly Ile Ser Lys Phe Val 95

Gln Lys Val Asn Glu Ile Gly Ile Tyr Leu Thr Asp **Cys** Met Glu Arg Ala Arg Glu 114

Val Ile Pro Arg Ser Gln His Gln Glu Thr Pro Val Tyr Leu Gly Ala Thr Ala Gly 133

Met Arg Leu Leu Arg Met Glu Ser Glu Glu Leu Ala Asp Arg Val Leu Asp Val Val 152

Glu Arg Ser Leu Ser Asn Tyr Pro Phe Asp Phe Gln Gly Ala Arg Ile Ile Thr Gly 171

Gln Glu Glu Gly Ala Tyr Gly Trp Ile Thr Ile Asn Tyr Leu Leu Gly Lys Phe Ser 190

Gln Lys Thr Arg Trp Phe Ser Ile Val Pro Tyr Glu Thr Asn Asn Gln Glu Thr Phe 209

Gly Ala Leu Asp Leu Gly Gly Ala Ser Thr Gln Val Thr Phe Val Pro Gln Asn Gln 228

Thr Ile Glu Ser Pro Asp Asn Ala Leu Gln Phe Arg Leu Tyr Gly Lys Asp Tyr Asn 247

Val Tyr Thr His Ser Phe Leu **Cys** Tyr Gly Lys Asp Gln Ala Leu Trp Gln Lys Leu 266

Ala Lys Asp Ile Gln Val Ala Ser Asn Glu Ile Leu Arg Asp Pro **Cys** Phe His Pro 285

Gly Tyr Lys Lys Val Val Asn Val Ser Asp Leu Tyr Lys Thr Pro **Cys** Thr Lys Arg 304

Phe Glu Met Thr Leu Pro Phe Gln Gln Phe Glu Ile Gln Gly Ile Gly Asn Tyr Gln 323

Gln **Cys** His Gln Ser Ile Leu Glu Leu Phe Asn Thr Ser Tyr **Cys** Pro Tyr Ser Gln 342

Cys Ala Phe Asn Gly Ile Phe Leu Pro Pro Leu Gln Gly Asp Phe Gly Ala Phe Ser 361

Ala Phe Tyr Phe Val Met Lys Phe Leu Asn Leu Thr Ser Glu Lys Val Ser Gln Glu 380

Lys Val Thr Glu Met Met Lys Lys Phe **Cys** Ala Gln Pro Trp Glu Glu Ile Lys Thr 399

Ser Tyr Ala Gly Val Lys Glu Lys Tyr Leu Ser Glu Tyr **Cys** Phe Ser Gly Thr Tyr 418

Ile Leu Ser Leu Leu Leu Gln Gly Tyr His Phe Thr Ala Asp Ser Trp Glu His Ile 437

His Phe Ile Gly Lys Ile Gln Gly Ser Asp Ala Gly Trp Thr Leu Gly Tyr Met Leu 456

Asn Leu Thr Asn Met Ile Pro Ala Glu Gln Pro Leu Ser Thr Pro Leu Ser His Ser 475

Thr Tyr Val Phe Leu Met Val Leu Phe Ser Leu Val Leu Phe Thr Val Ala Ile Ile 494

Gly Leu Leu Ile Phe His Lys Pro Ser Tyr Phe Trp Lys Asp Met Val 510

Fig. 1

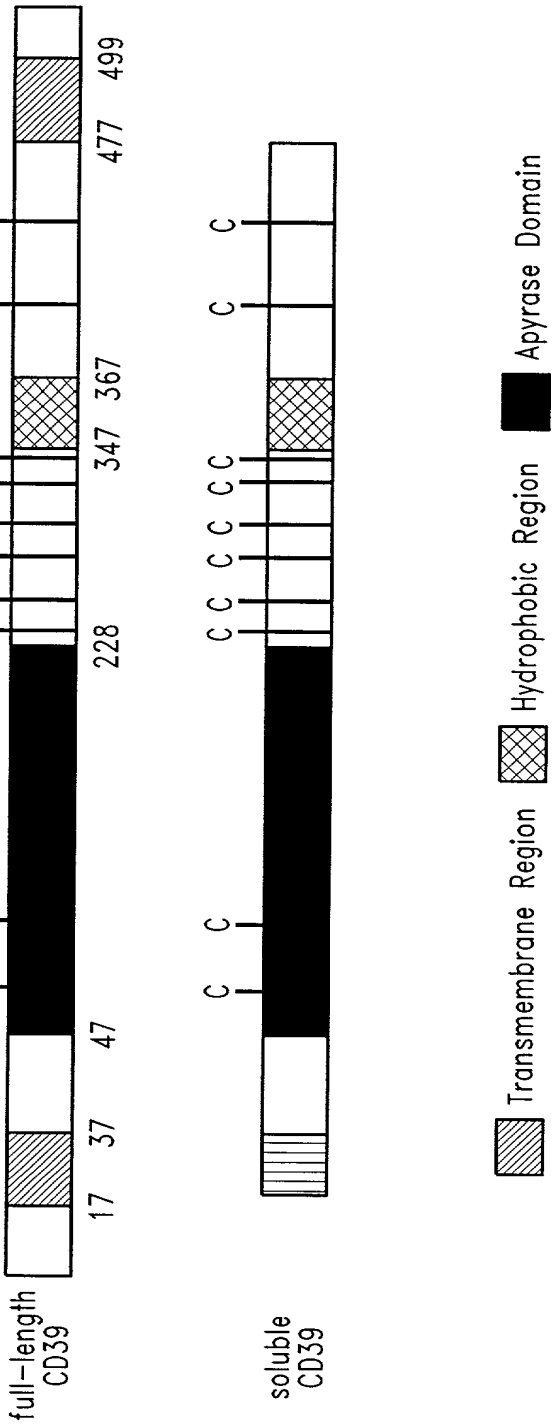
full-length CD39
soluble CD39
17
37
47
228
347
367
477
499
Transmembrane Region
Hydrophobic Region
Apyrase Domain
Flag and IL-2 leader

Fig. 2

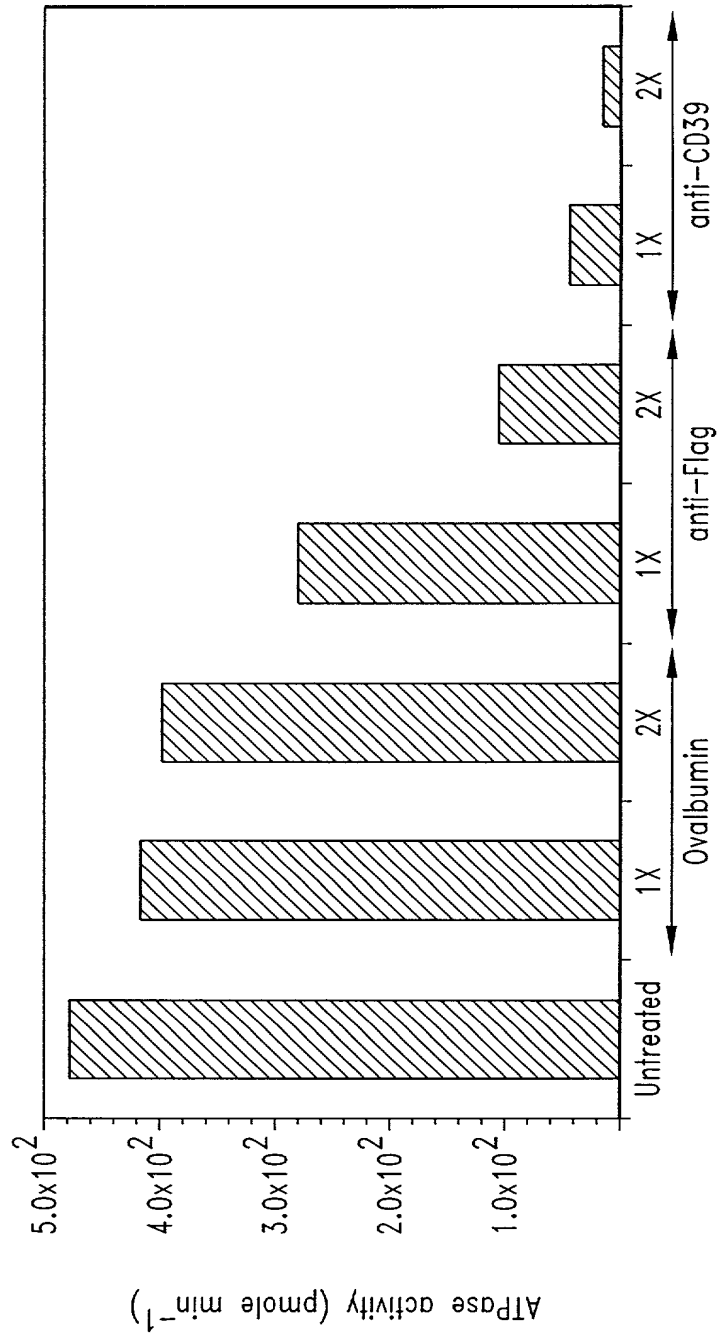
ATPase activity (pmole min^{-1})
5.0x10^2
4.0x10^2
3.0x10^2
2.0x10^2
1.0x10^2
Untreated
1X
2X
Ovalbumin
1X
2X
anti-Flag
1X
2X
anti-CD39

Fig. 3

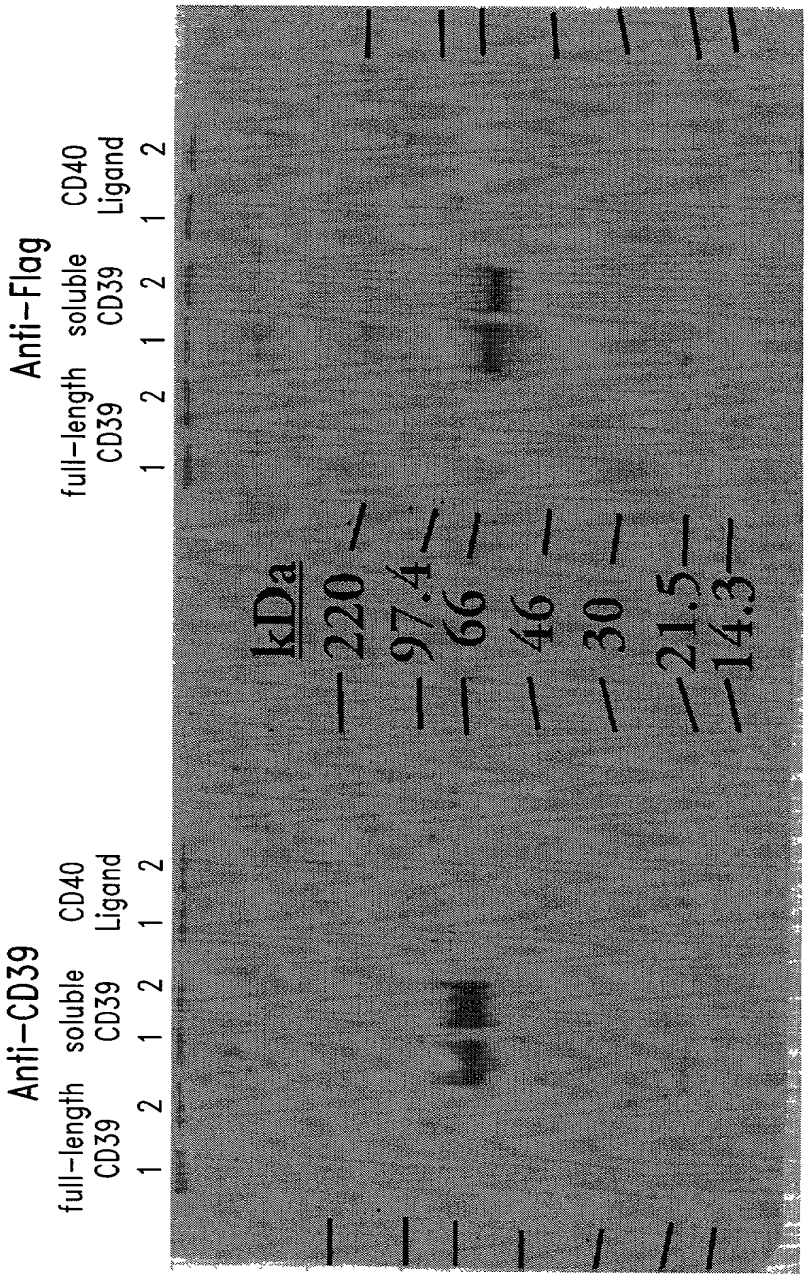
Anti-CD39
full-length CD39
soluble CD39
CD40 Ligand
1 2 1 2 1 2
Anti-Flag
full-length CD39
soluble CD39
CD40 Ligand
1 2 1 2 1 2
kDa
220
97.4
66
46
30
21.5
14.3

Fig. 4

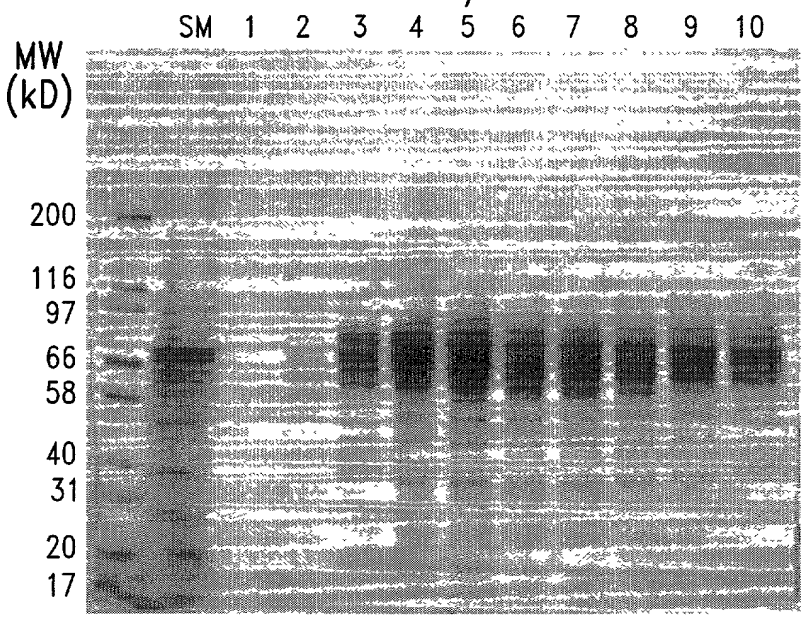
SM 1 2 3 4 5 6 7 8 9 10
MW (kD)
200
116
97
66
58
40
31
20
17

Fig. 5A

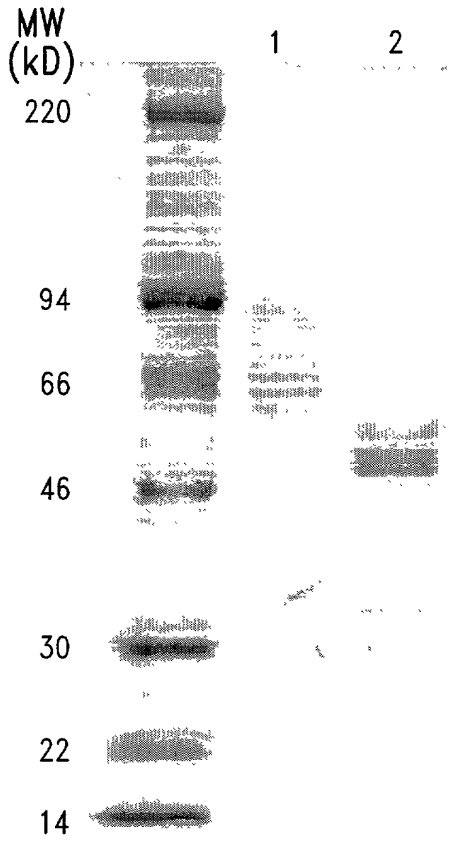
MW (kD)
1
2
220
94
66
46
30
22
14

Fig. 5C

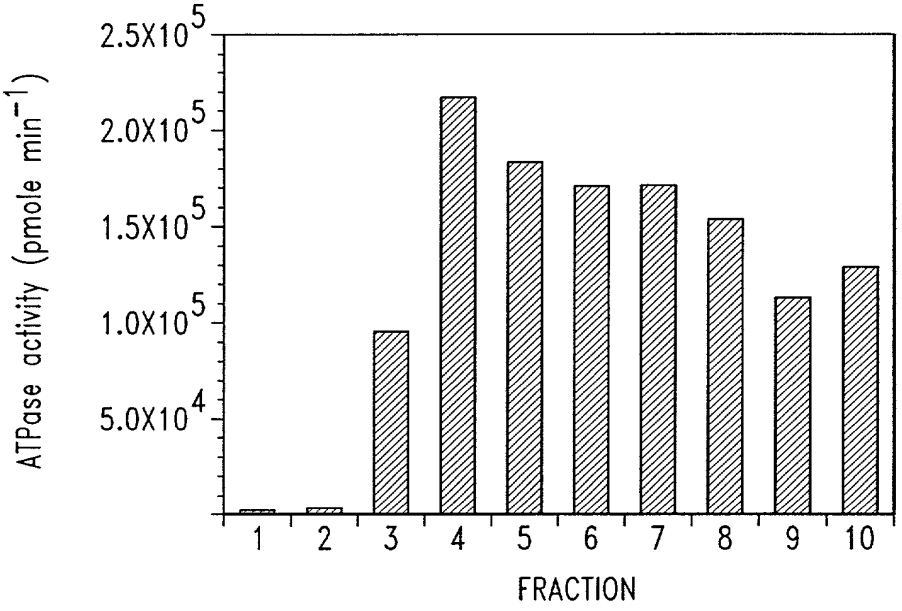
2.5X10^5
2.0X10^5
1.5X10^5
1.0X10^5
5.0X10^4
ATPase activity (pmole min^-1)
1
2
3
4
5
6
7
8
9
10
FRACTION

Fig. 5B

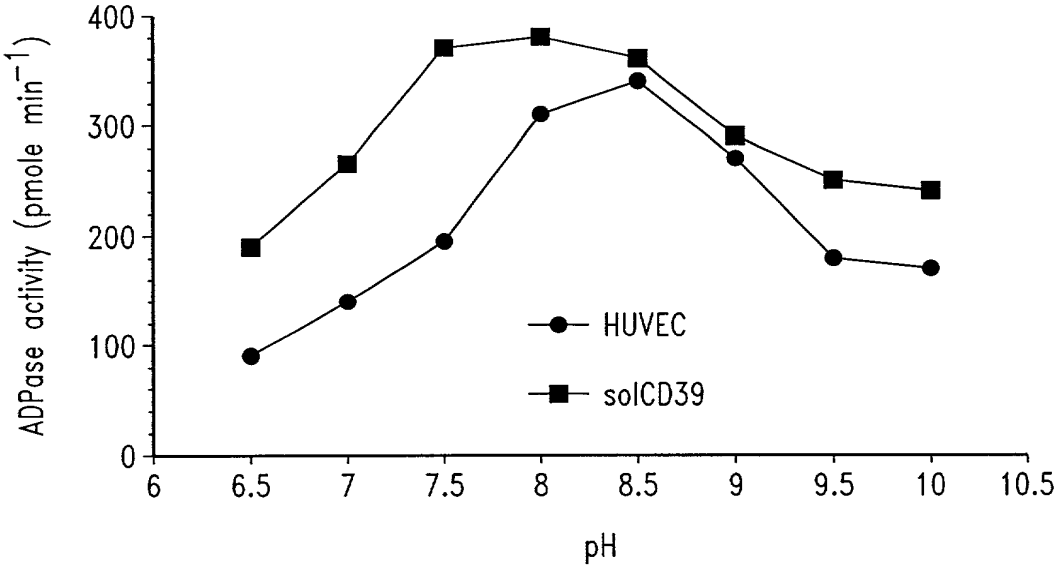
ADPase activity (pmole min^{-1})
400
300
200
100
0
6
6.5
7
7.5
8
8.5
9
9.5
10
10.5
pH
HUVEC
solCD39

Fig. 6A

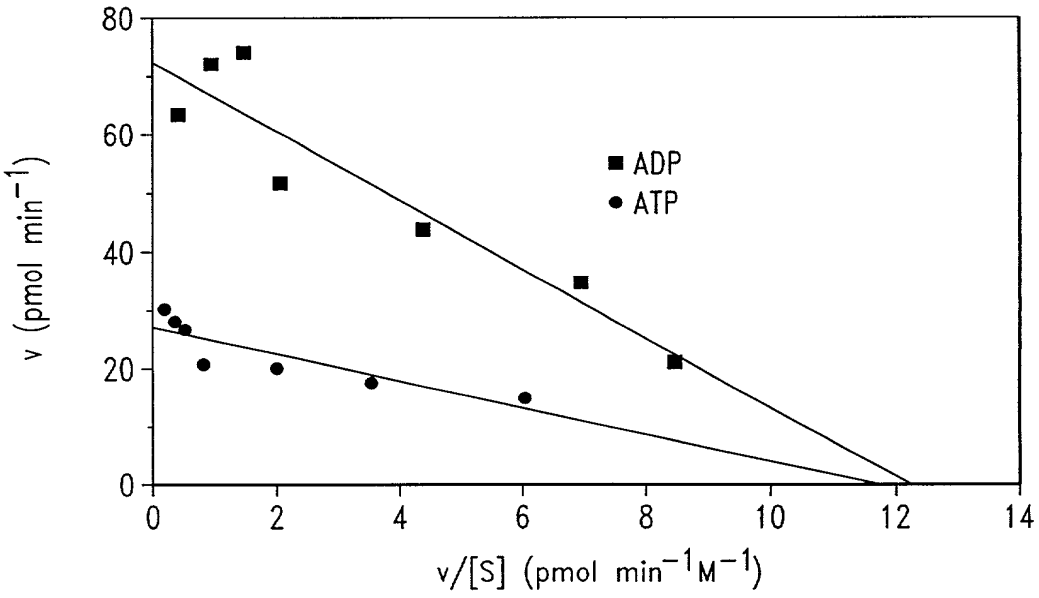
v (pmol min^{-1})
80
60
40
20
0
0
2
4
6
8
10
12
14
v/[S] (pmol min^{-1}M^{-1})
ADP
ATP

Fig. 6B

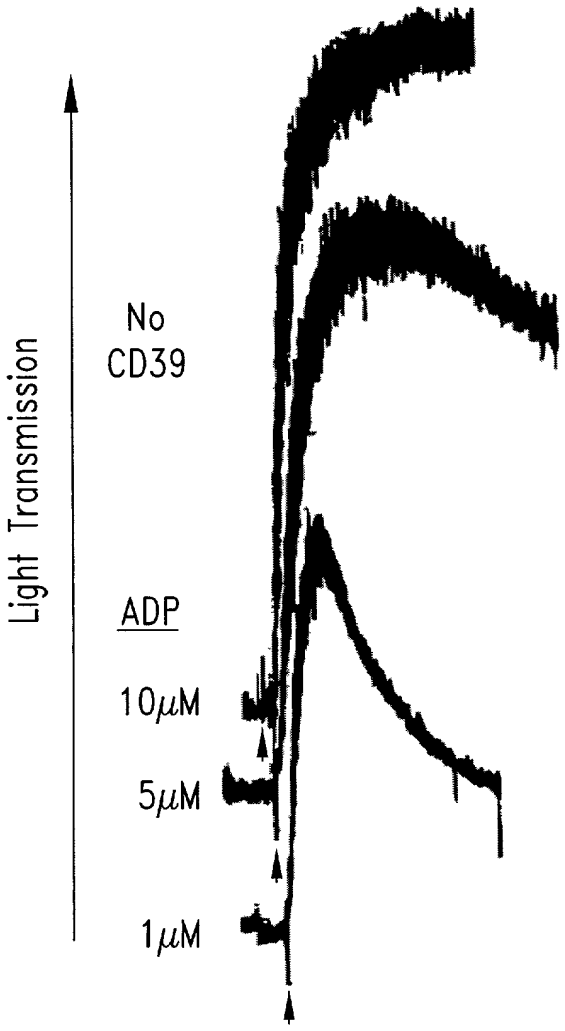
Light Transmission
No
CD39
ADP
10μM
5μM
1μM

Fig. 7A

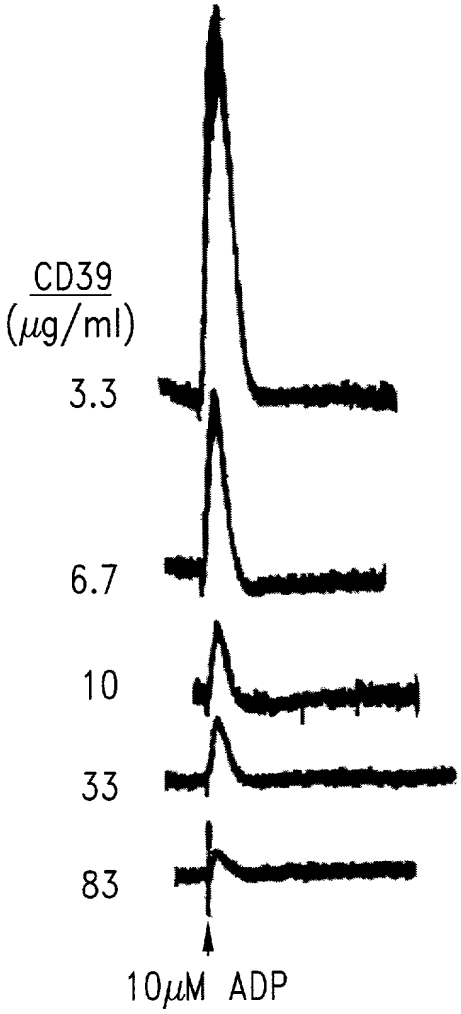
CD39
(μg/ml)
3.3
6.7
10
33
83
10μM ADP

Fig. 7B

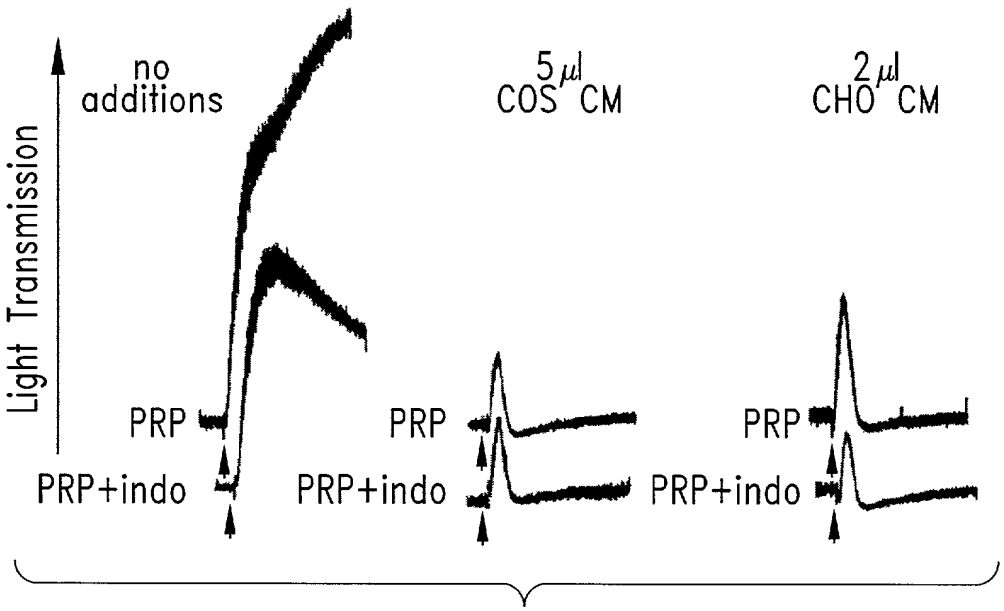

Fig. 8A

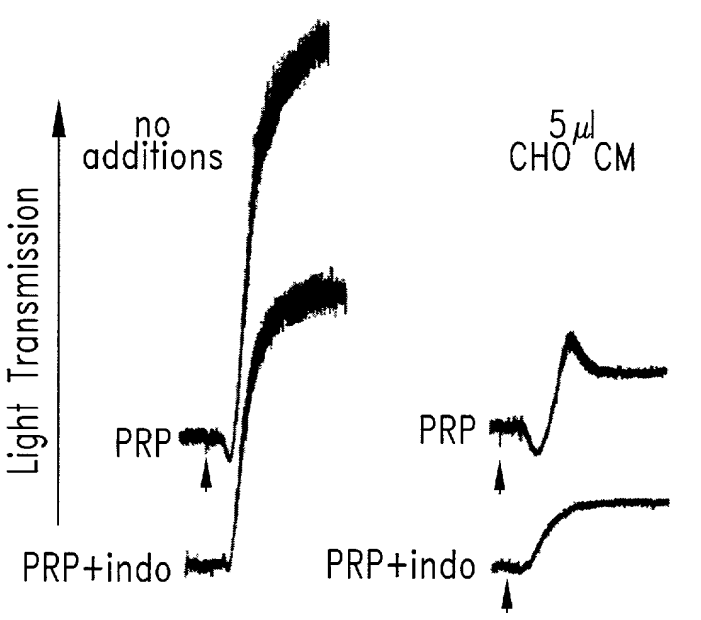

Fig. 8B

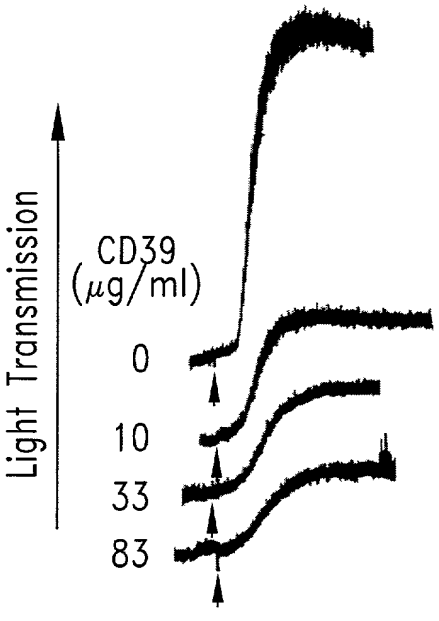

Fig. 8C

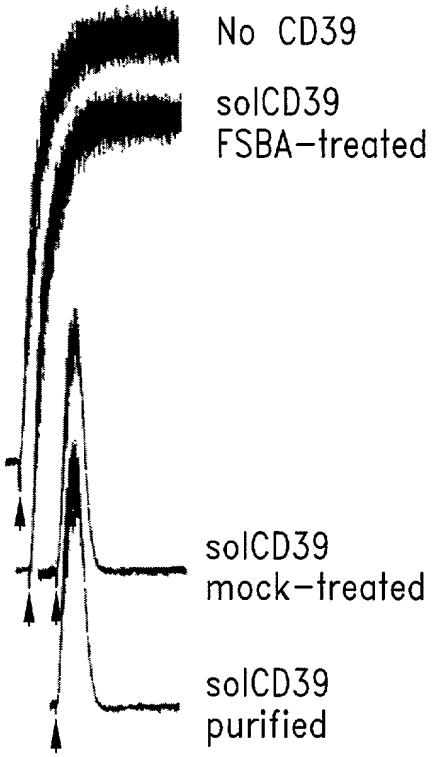

Fig. 9A

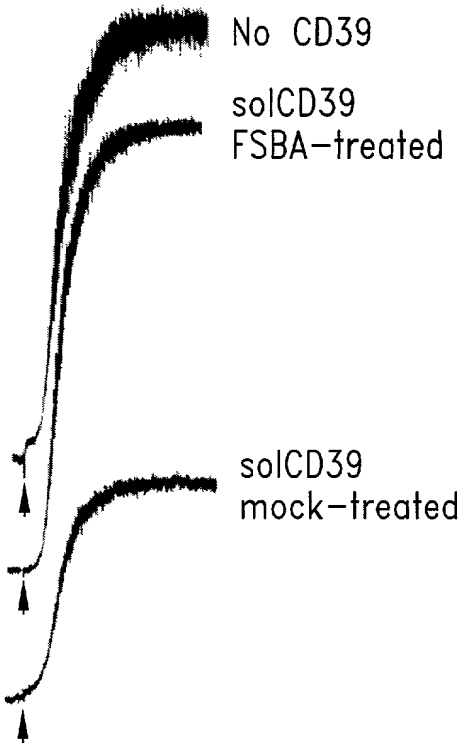

Fig. 9B

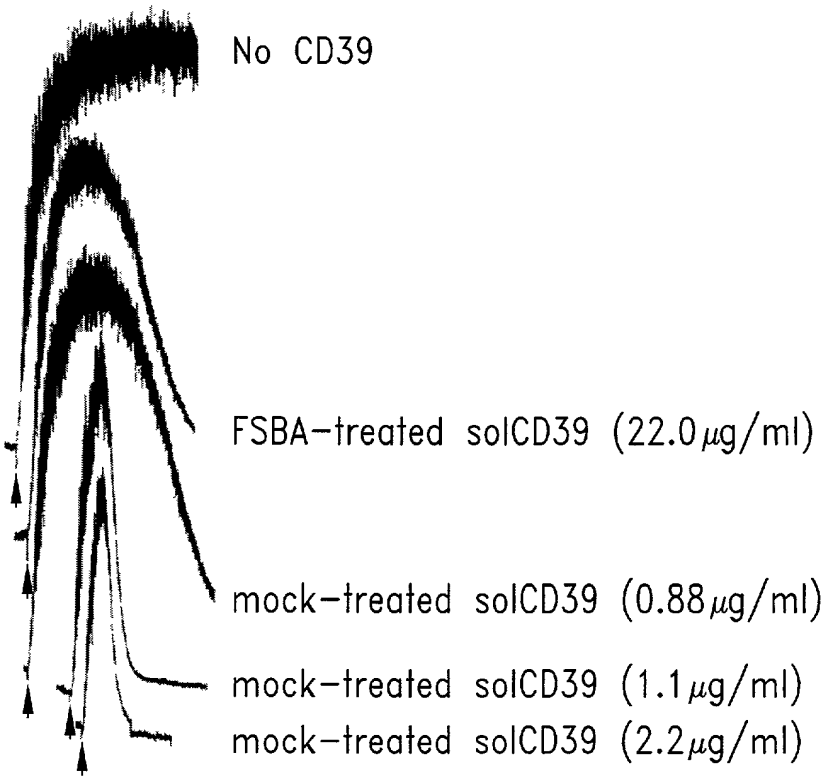

Fig. 9C

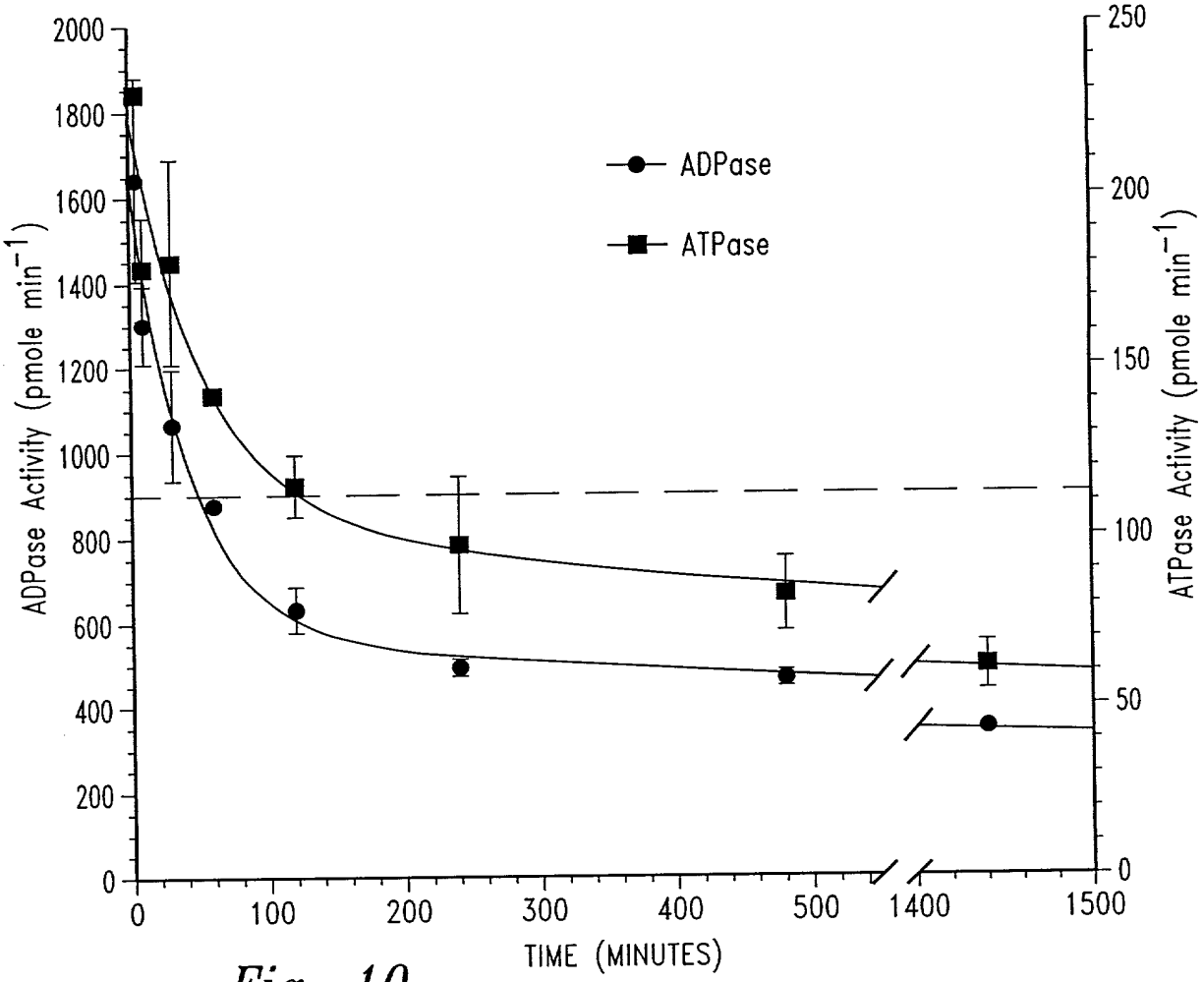
ADPase
ATPase
ADPase Activity (pmole min^{-1})
ATPase Activity (pmole min^{-1})
TIME (MINUTES)
0
200
400
600
800
1000
1200
1400
1600
1800
2000
0
50
100
150
200
250
0
100
200
300
400
500
1400
1500

Fig. 10

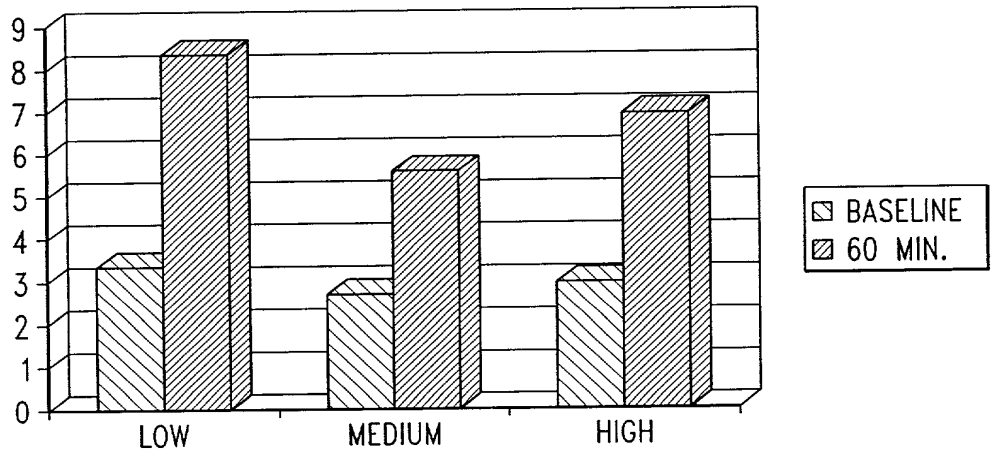
0
1
2
3
4
5
6
7
8
9
LOW
MEDIUM
HIGH
BASELINE
60 MIN.

Fig. 11

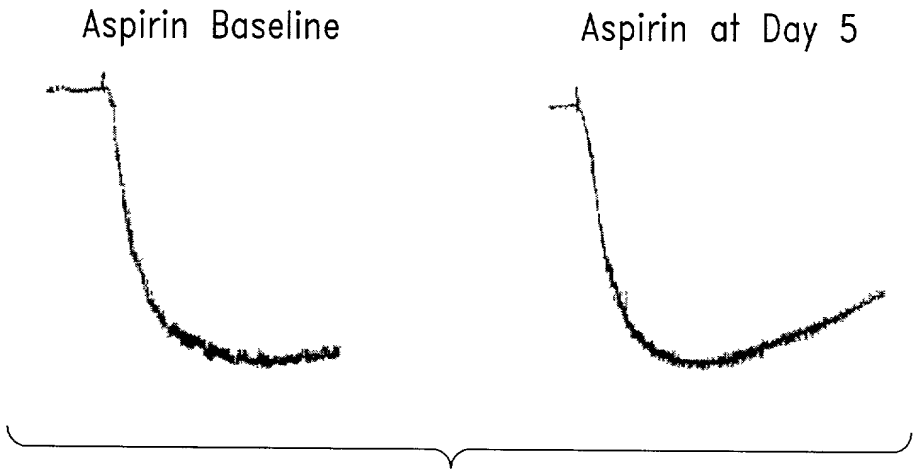

Fig. 12A

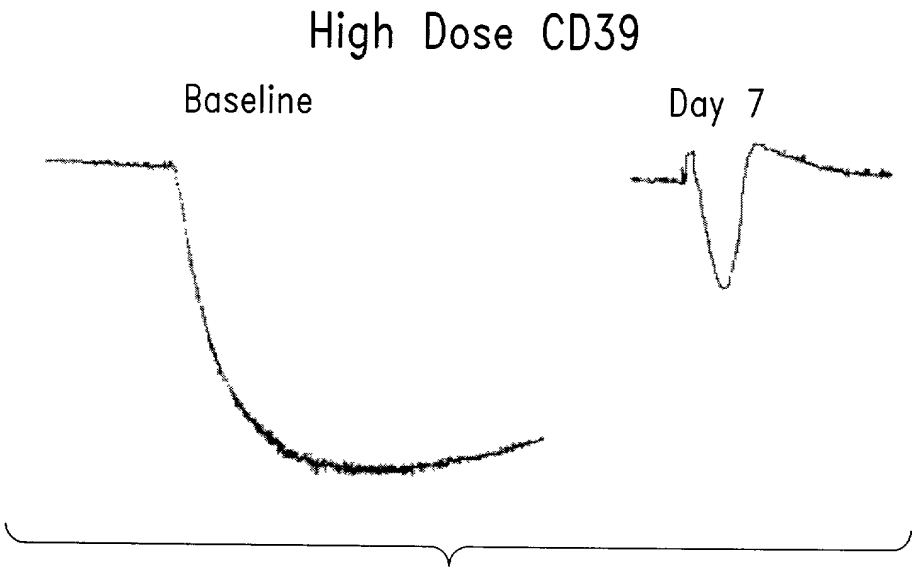

Fig. 12B

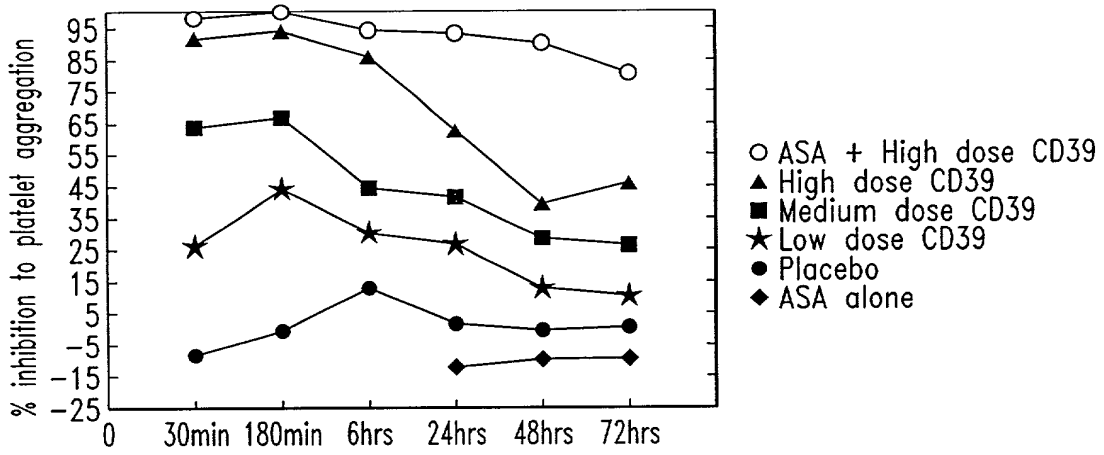
% inhibition to platelet aggregation
95
85
75
65
55
45
35
25
15
5
−5
−15
−25
0
30min
180min
6hrs
24hrs
48hrs
72hrs
ASA + High dose CD39
High dose CD39
Medium dose CD39
Low dose CD39
Placebo
ASA alone

Fig. 13

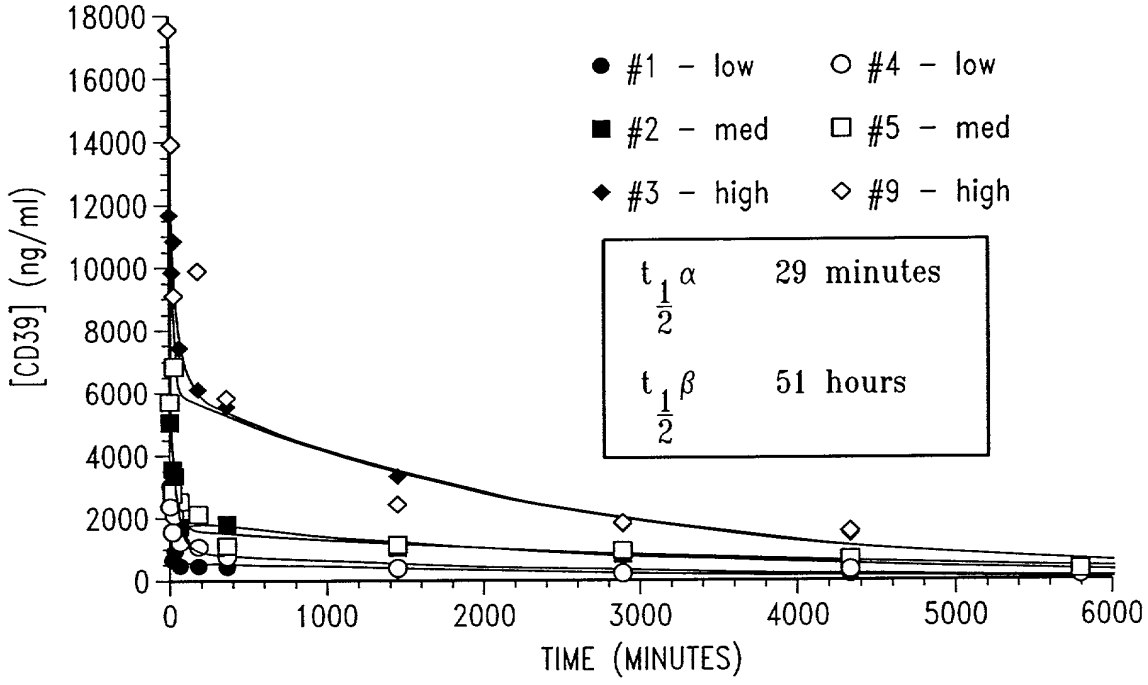
[CD39] (ng/ml)
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
1000
2000
3000
4000
5000
6000
TIME (MINUTES)
#1 – low
#4 – low
#2 – med
#5 – med
#3 – high
#9 – high
$t_{\frac{1}{2}}\alpha$ 29 minutes
$t_{\frac{1}{2}}\beta$ 51 hours

Fig. 14

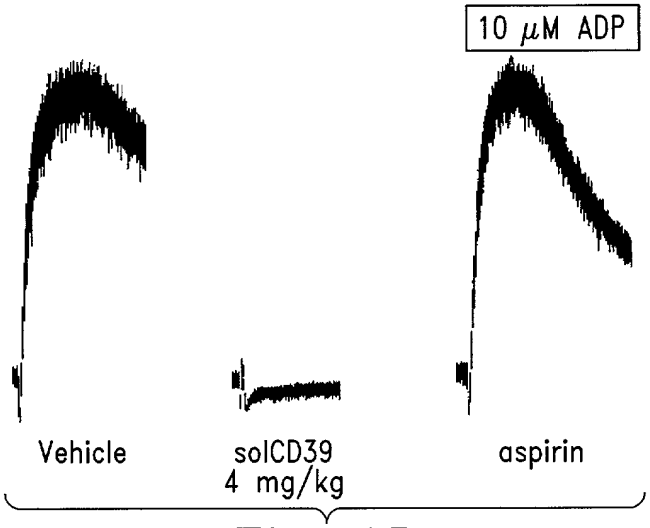

Fig. 15A

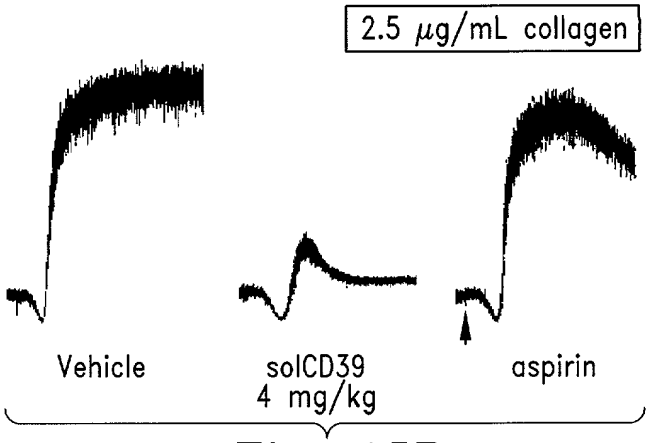

Fig. 15B

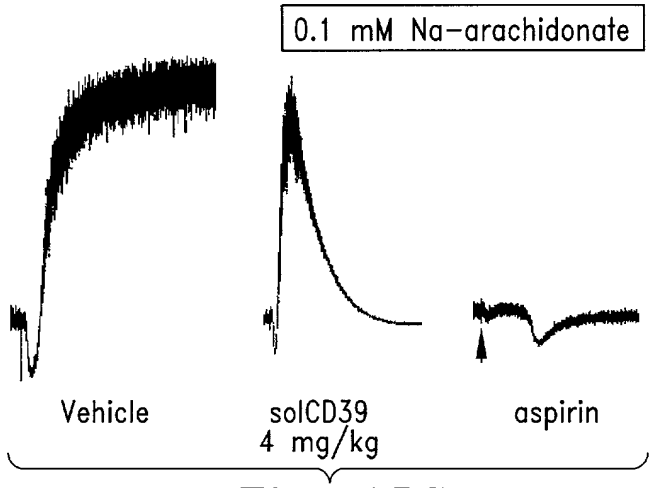

Fig. 15C

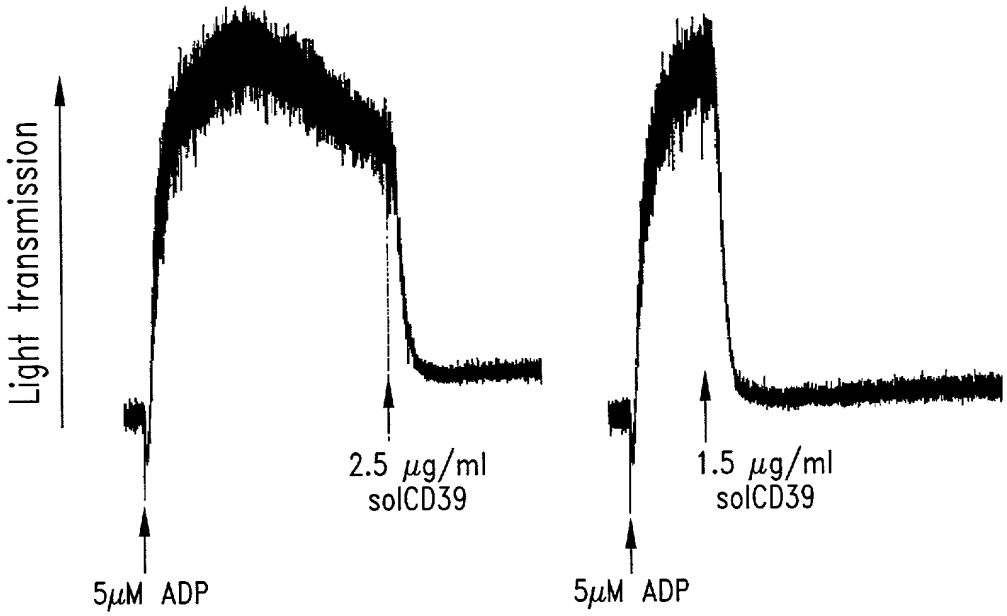

Fig. 16

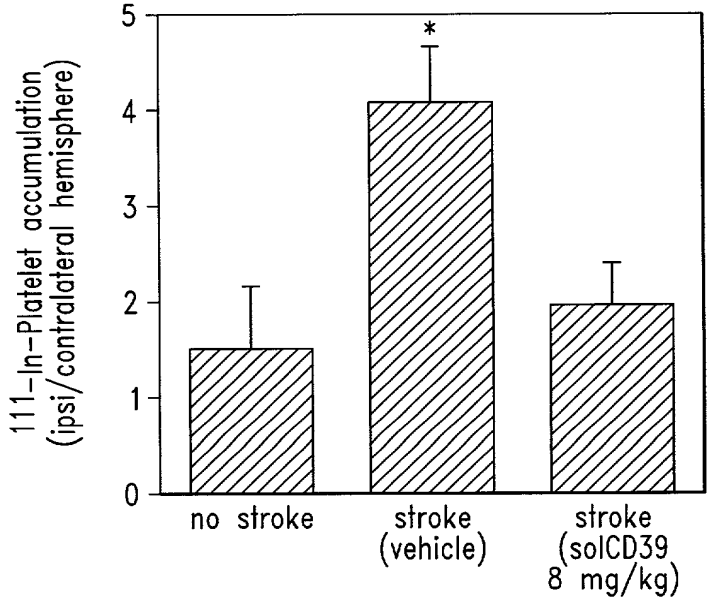

Fig. 17A

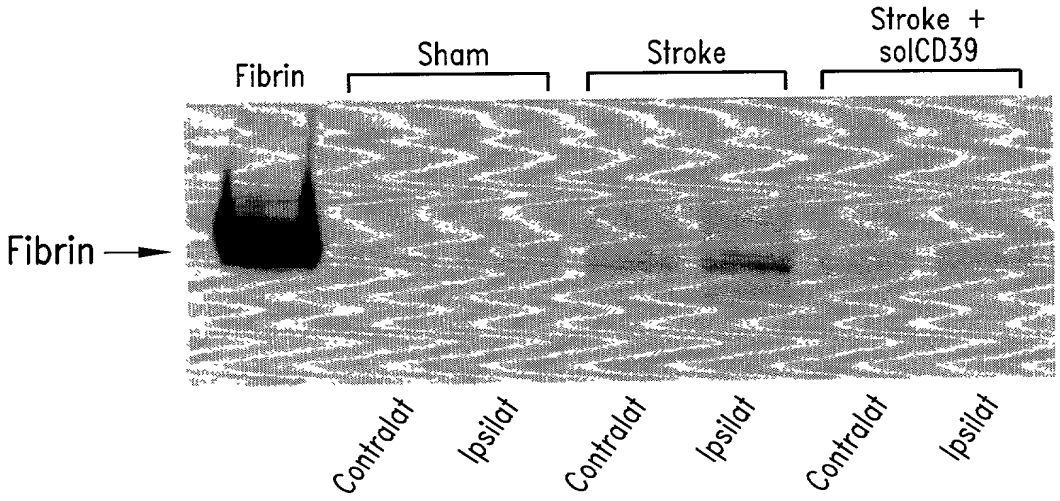
Fibrin
Sham
Stroke
Stroke +
solCD39
Fibrin
Contralat
Ipsilat
Contralat
Ipsilat
Contralat
Ipsilat

Fig. 17B

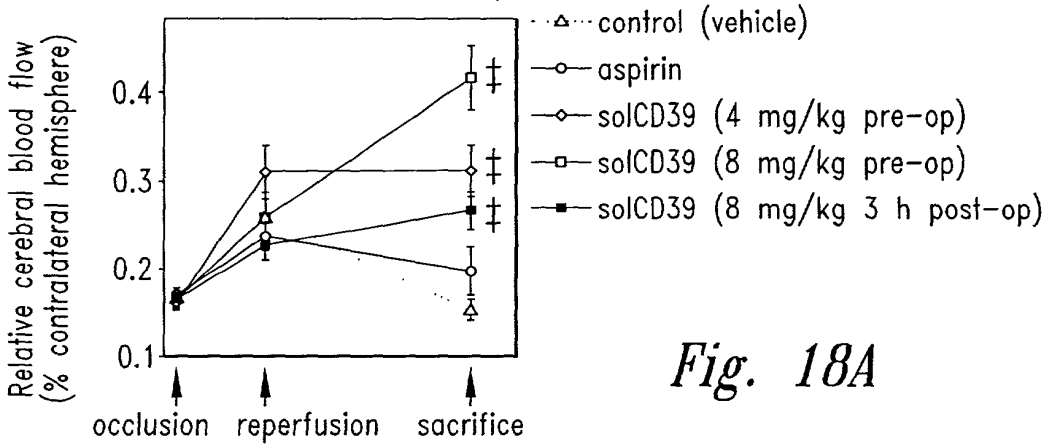

Fig. 18A

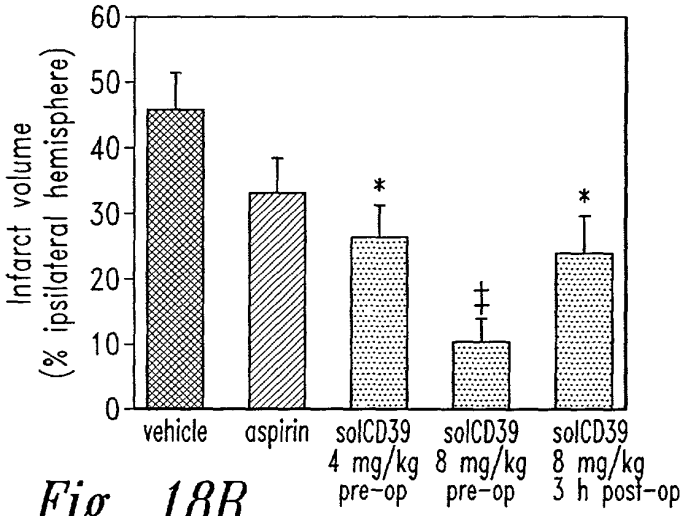

Fig. 18B

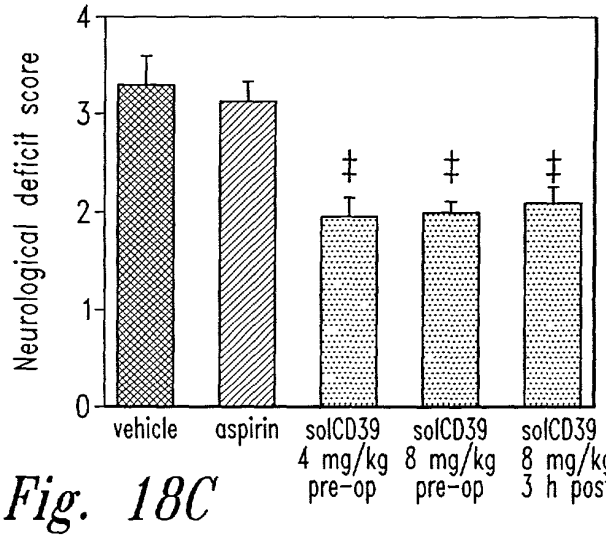

Fig. 18C

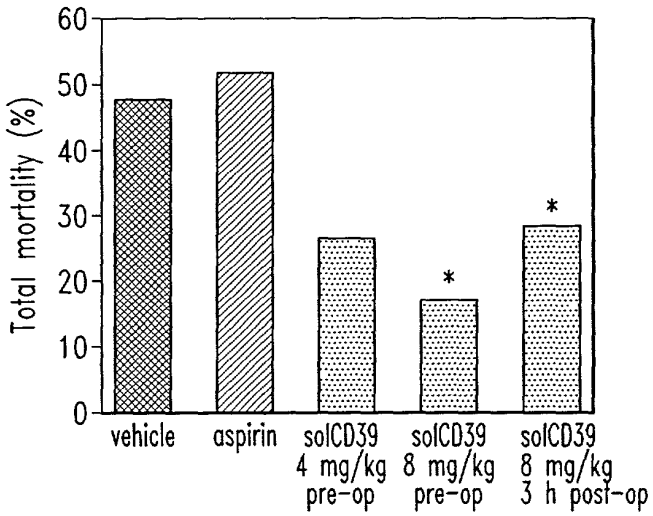

Fig. 18D

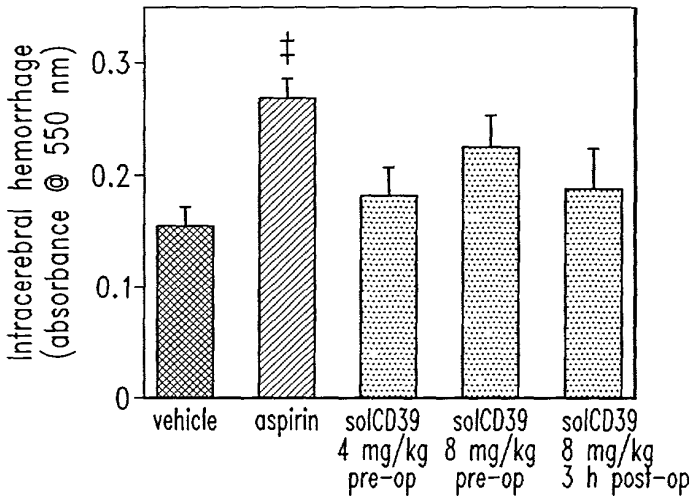

Fig. 18E

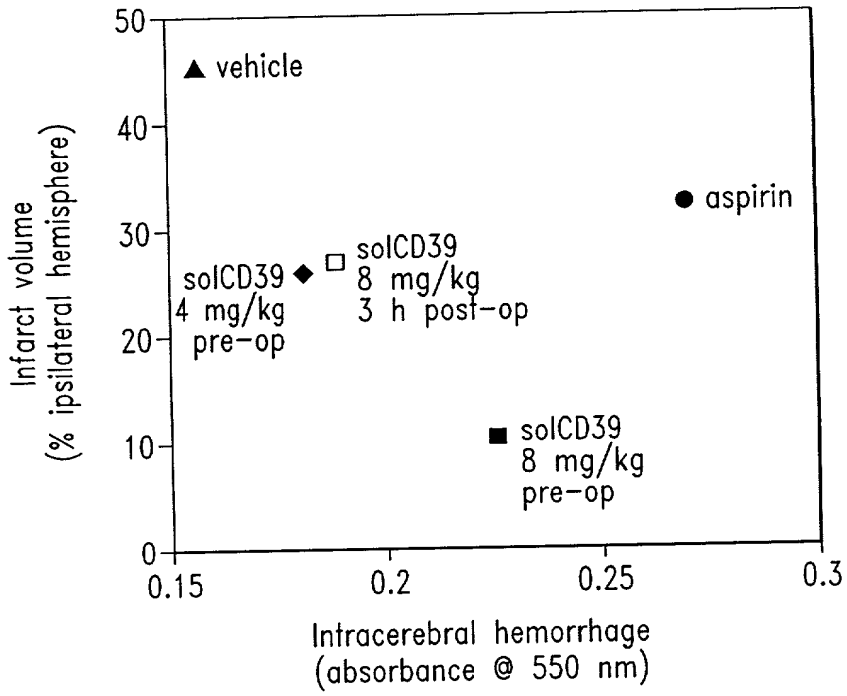

Fig. 19

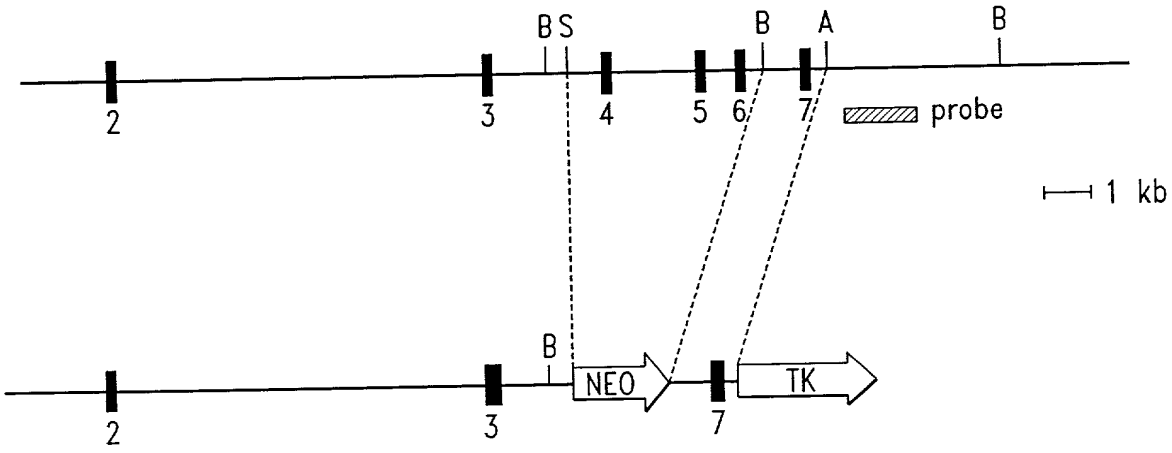

Fig. 20A

Fig. 20B

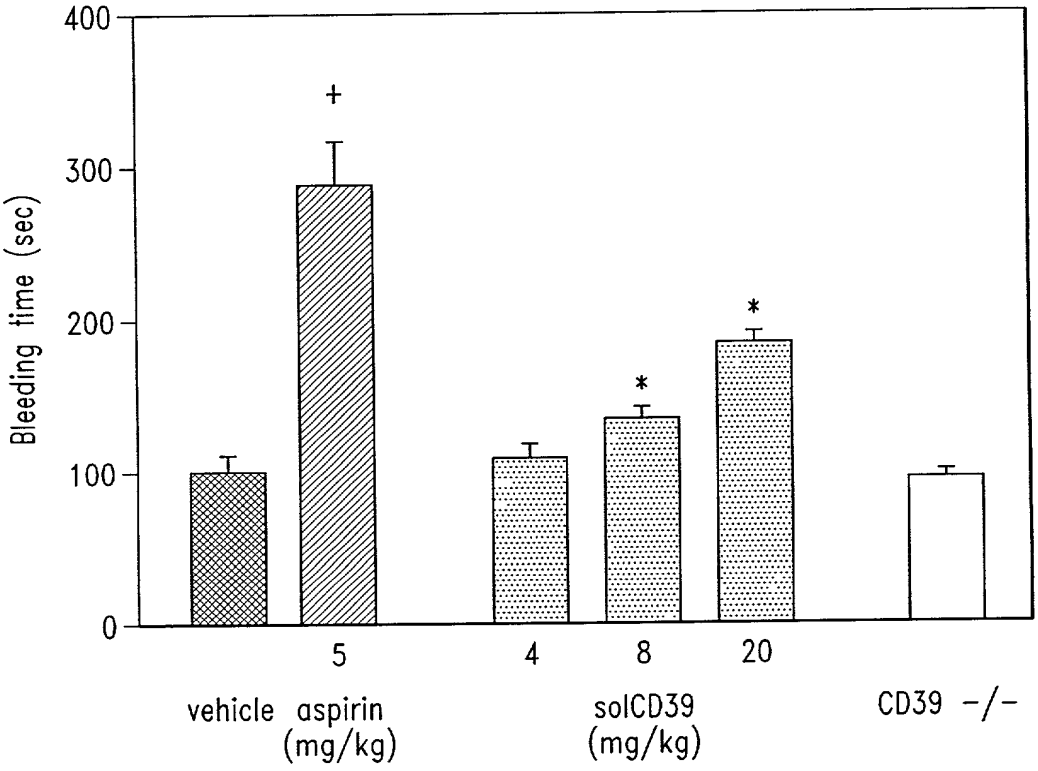
400
300
200
100
0
Bleeding time (sec)
+
*
*
5
4
8
20
vehicle
aspirin
(mg/kg)
solCD39
(mg/kg)
CD39 -/-

Fig. 21

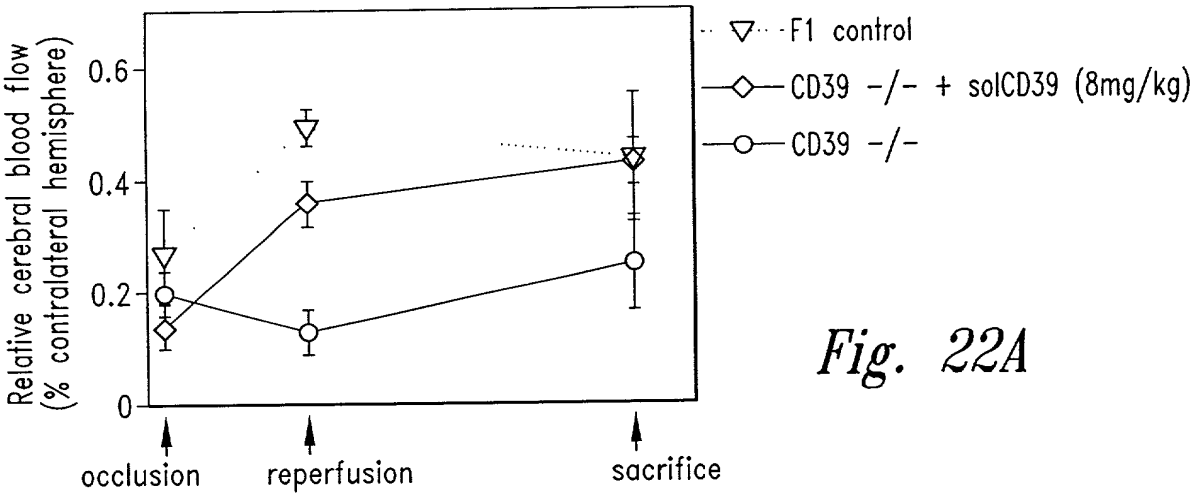

Fig. 22A

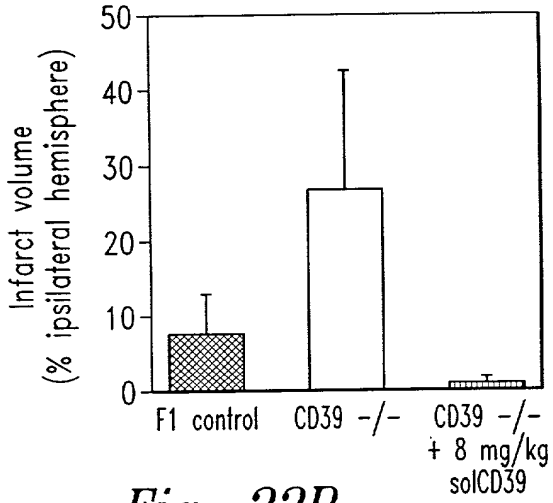

Fig. 22B

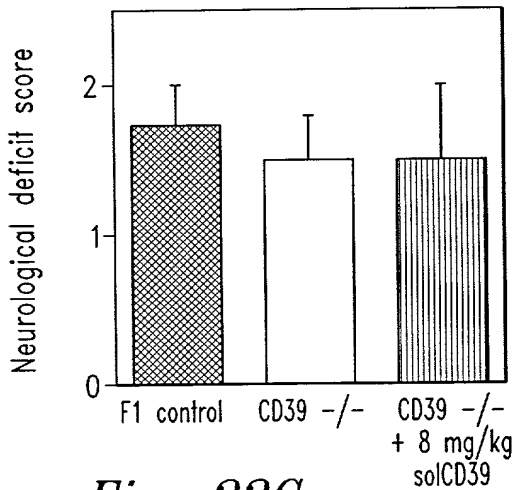

Fig. 22C

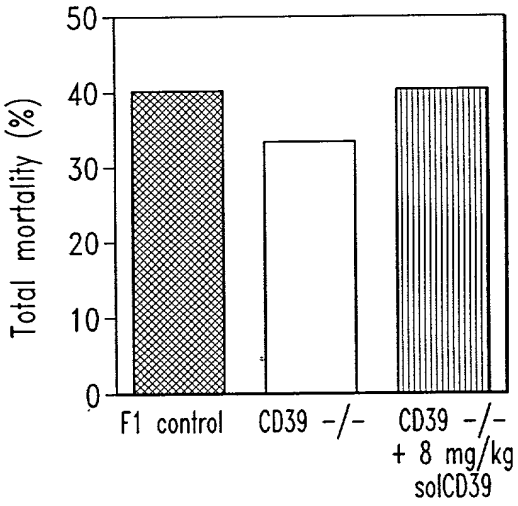

Fig. 22D

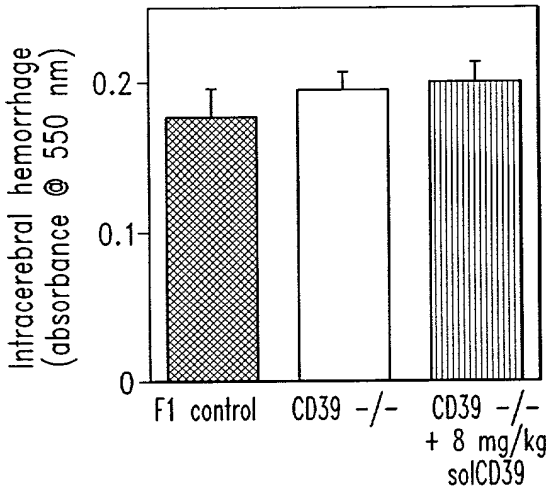

Fig. 22E

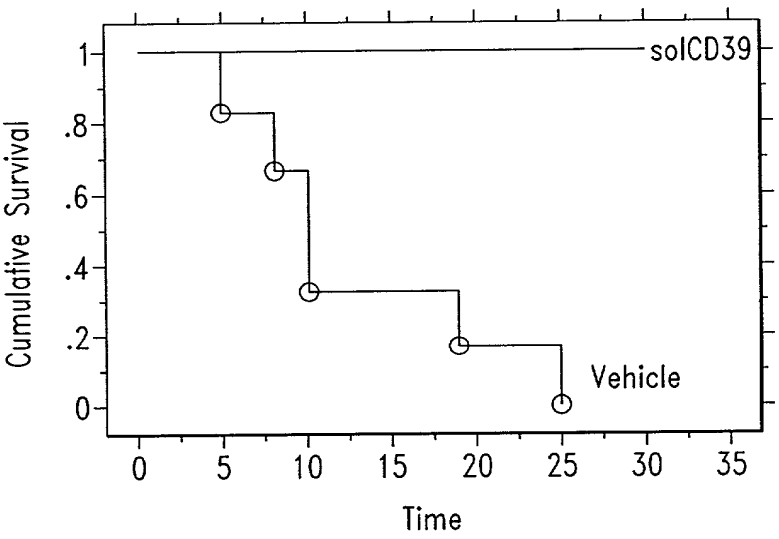

Fig. 23

Human CD39 (amino acids 1-69 of SEQ ID NO:2)
MEDTKESNVK TFCSKNILAI LGFSSIIAVI ALLAVGLTQN KALPENVKYG IVLDAGSS...
|
MATSWGTVFF MLVVSCVCSA VSHRNQQTWF EGIFLSSMCP INVSASTLYG IMFDAGST...
Human CD39-L4 (SEQ ID NO:31)

Fig. 24